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Benchmarking on Cost Structure

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Benchmarking on Cost Structure

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I-1 Introduction to this work

The aim of this work is to investigate the current production processes of ### and the production situation of domestic ### producers, from aspects of production costs and the profit of certain major Chinese ### manufacturers. The production process, production cost and profit of Zhejiang ####, Zhejiang ####, and Zhejiang ####, the major ### producers in China, will be analyzed. Based on these works, the strength and weakness of Chinese ### manufacturers will be also analyzed.

Briefly, the whole work of benchmarking of ### is divided into several stages:

◆ Preparative work

- ✓ Extensive study on ### process with information from our experience, from literatures, from patents, from Chinese manufacturers and Professor ##### Chen, the main researcher.
- ✓ To set up the production model of ### in China based on the above information.
- ✓ To pre-estimate of unit consumption and production cost in China based on the production model.

◆ Discussion with manufacturers & information verification

- ✓ To carry out site visit with Professor ##### Chen in order to obtain some information on technology and production cost.
- ✓ To make telephone interview with some active domestic ### manufacturers and ### derivatives producers in order to obtain some information of production like raw material cost, management situation, market information
- ✓ To verify the information obtained from the patents and literatures with the information obtained from the factory
- ✓ To modify the model established

◆ Production cost estimation

- ✓ To verify the model and raw material cost and estimate the total production cost of Chinese ### producers and compare this to the actual situation of the factory.
- ✓ To estimate the net profit of Chinese producers.

I-2 Theoretical Analysis

I-2.1 Technology Research

The main research institute is Chemical Department of Fudan University and the chief researcher is Professor ##### Chen. He has been researching on ### for over ten years. All of the domestic technologies are directly or indirectly from him.

He developed the chemical synthesis technology of ###. The yield is increased from 25% of Roche to

40~50%. The cost is reduced from RMB3,000~4,000/kg in 2003 to lower than RMB 2,000/kg in 2008.

The domestic development is in the process of improving product quality, increasing yield, saving energy, reducing production cost and how to produce ### in room temperature and atmospheric pressure.

There are three main kinds of production technologies in the world, including extraction method, fermentation method and chemical synthetic method. In China, only chemical synthetic method is applied in commercial production.

I-2.2 Extraction Method

Natural ### mostly exists in the eggs, milk and animal liver, etc. from which ### can be extracted.

Through alumina chromatogram extraction process, ### is obtained via distillation in vacuum.

This pathway is mainly used to produce biochemical reagent grade ###. Its yield is low and the cost is high.

I-2.3 Fermentation Method

is produced via the fermentation of microorganism. This process is difficult to operate. The yield is not high and the product quality is not stable. The main raw materials are a variety of enzymes.

The main process is

Heptanoic acid → heptanoyl coenzyme A → 7-keto-8-amino pelargonic acid → 7,8-diamino pelargonic acid → desulphating ### → ###

As to feed-grade ###, the production steps include preparation of culture medium, seed fermentation, raw materials fermentation, concentration and drying.

As to pharmaceutical-grade ###, the production steps include preparation of culture medium, seed fermenting, raw materials fermenting, film filtration, chromatogram separation, concentration, crystal, separation and drying.

The raw materials include glucose, dipotassium hydrogen phosphate, magnesium sulphate, potassium chloride, ferrous sulphate, yeast extract, pimelic acid, etc.

Based on the capacity of 6t/a, the energy consumption of ###, including 1t/a pharmaceutical grade and 250t/a 2% feed grade, is as follows:

Table I-2.3-1 Energy consumption of ### production in fermentation method

	Feed Grade 2%	Pharmaceutical grade 97% min.
Water	xxx	xxx
Steam	xxx	xxx
Electricity	xxx	xxx

Source: CCM

The ferment time is 24 hours. The total yield is 80-90%.

Zhao Wang, Professor of Zhejiang University of Technology, is researching on ferment method now. At the moment, the yield rate of ferment method is very low, which can not be transferred into commercial production. But he is researching how to recycle some by-product in the production of ###.

In production of (4R,5S)-1,3-Dibenzyl-4-{N-[(1S,2S)-(+)-threo-1-hydroxymethyl-2-(p-Nitrobenzylic)-2-hydroxyethyl]aminomethyl}-5-hydroxymethyl-tetrahydroimidazole-2-ketone ((4R,5S)), there is a by-product: (4S, 5R)- 1,3-Dibenzyl-4-{N-[(1S,2S)-(+)-threo-1-hydroxymethyl-2-(p-Nitrobenzylic)-2-hydroxyethyl]aminomethyl}-5-hydroxymethyl-tetrahydroimidazole-2-ketone((4S, 5R)) which can not be used in chemical synthesis method. Pr. Zhao Wang is researching how to transfer (4S, 5R) into (4R,5S) by fermentation method. Now, the transfer rate is only 20%. He will continue to increase the transfer rate.

I-2.4 Chemical Synthetic Method

At the moment, in China, all chemical pathways begin from cyclic acid. ### is synthesized via several reactions, including condensation with chloroacetic acid, acylation, esterification, sulfidation reaction, Grignard, carboxylation reaction, cyclization, etc.

In the chemical synthetic method of ### production, some toxic chemicals, such as potassium cyanide and phosgene, are needed in the Sternbach process, which will cause pollution to the environment.

However, Chinese manufacturers do not use these highly toxic chemicals. Of course, there is no doubt that the production generates some pollution too, as it needs to use many kinds of organic solvent.

➤ Sternbach Process

This process has 13 steps and the yield is 25%.

This process has some shortcomings, especially the thio reaction of oxygen in furan nucleus of the (3aS, 6aR) -1,3-dibenzyl-tetrahydro-4H-thieno [3,4-d] imidazole-2, 4-(1H)-dione. The thio-agent potassium thioacetate is synthesized by thioacetic acid and potassium hydride in the temperature of -78°C, which is difficult to operate the reaction.

It is difficult to split in the production process. In Sternbach process, (+)-ephedrine or 1,3-diphenylethylamine is often used as split agent. In the industrial production, these split agents have many shortcomings, such as high cost, short supply, low split yield, etc.

At present, the overseas companies are still using sternbach process to produce ###, but there are still many problems in this process. Although the foreign experts have tried many different ways either from the chemical reaction or from the industrial synthesis to solve the problems of this process, there's little improvement. For example, the raw material is difficult to obtain and it is also difficult for the preparation of C5. What's more, the yield of debenzylation is very low. Maybe, this is why there's little progress for the development of d-### in China with the simulated sternbach process from abroad.

➤ **Domestic Process**

Professor ##### Chen, a famous professor of Fudan University, has researched on the industrial synthesized production of ### for over 10 years and he will go on researching ### in all his life. There are two kinds of ### production processes in China and CCM names them as Process A and Process B hereinafter. Both of Process A and Process B are developed by Chen. Process A was developed in 1999 and it was sold to Zhejiang #####. Process B was sold to Zhejiang ##### in 2002 and the technology was leaked to Zhejiang ##### in 2003.

I-2.4.1 Process A

➤ **Introduction**

Process A is used by Zhejiang ##### and its brief production pathway is as follow:

.....

Source: CCM

Figure II-2.4.1-1 Flow chart of Process A

.....

Source: CCM

Process A was developed by Professor ##### Chen in 1999 and Zhejiang ##### put it into commercial production in 2001. As Zhejiang ##### did not pay money to Professor ##### Chen for the technology, Professor ##### Chen does not help Zhejiang ##### to upgrade this technology. Now the technology in Zhejiang ##### is outdated.

The research team of Zhejiang #####, with its leader-Mr. Jia#####i Chen, has done a lot to improve it. But this process is still laggard in China.

Table I-2.4.1-1 Yield rate of each reaction of Process A

Reaction NO.	Reaction name	Yield rate
A	Acylation ammoniation	xxx
B	Reduction reaction	xxx
C	Hydrolysis	xxx

D	Sulfidation reaction	xxx
E	Grignard	xxx
F	Dehydration reaction	
G	Reduction reaction	
H	N//A	
I	Condensation reaction	xxx
J	Ring-opening reaction	xxx
K	Ring-closing reaction	xxx

Source: CCM

The yield rate of each reaction mentioned above are quite satisfying except for the reaction B, which makes the total yield rate reach 31.06% based on cyclic Acid.

However, this technology has the following disadvantages:

1. Total yield rate is low, only 31.06%.
2. It needs more labors, longer reaction times and higher consumption of water, electricity and gas.
3. It needs many kinds of solvents, which make it difficult to recover solvents, and it not only wastes a lot of solvents, but also increases environmental protection cost.

➤ Production model

Based on the unit price of materials obtained in September 2008, CCM calculated the approximate cost of the raw materials.

Table I-2.4.1-2 Estimation on raw material cost for Process A

No.	Raw Materials	Consumption, Unit / kg ###	Unit	Price, RMB/Unit	Unit cost, RMB/kg ###
1	####	xxx	kg	xxx	xxx
2	####	xxx	kg	xxx	xxx
3	####	xxx	kg	xxx	xxx
4	####	xxx	kg	xxx	xxx
5	####	xxx	kg	xxx	xxx
6	####	xxx	kg	xxx	xxx
7	####	xxx	kg	xxx	xxx
8	####	xxx	L	xxx	xxx
9	####	xxx	L	xxx	xxx
10	####	xxx	kg	xxx	xxx
11	####	xxx	L	xxx	xxx
12	####	xxx	kg	xxx	xxx
13	####	xxx	kg	xxx	xxx
14	####	xxx	kg	xxx	xxx
15	####	xxx	kg	xxx	xxx

16	####	xxx	kg	xxx	xxx
17	####	xxx	kg	xxx	xxx
18	####	xxx	g	xxx	xxx
19	####	xxx	g	xxx	xxx
20	####	xxx	L	xxx	xxx
21	####	xxx	L	xxx	xxx
22	####	xxx	L	xxx	xxx
23	####	xxx	L	xxx	xxx
24	####	xxx	L	xxx	xxx
25	####	xxx	kg	xxx	xxx
26	####	xxx	L	xxx	xxx
27	####	xxx	kg	xxx	xxx
28	####	xxx	kg	xxx	xxx
29	####	xxx	L	xxx	xxx
30	####	xxx	kg	xxx	xxx
31	####	xxx	L	xxx	xxx
32	####	xxx	L	xxx	xxx
33	####	xxx	kg	xxx	xxx
34	####	xxx	kg	xxx	xxx
35	####			xxx	xxx
	Total			xxx	xxx

Note: According to the boiling point and polarity of solvents, CCM gives different solvent 70%~ 90% recycle rate. The recycle rate of Pd-D296 is 90%.

Source: CCM

I-2.4.2 Process B

➤ Introduction

This process also begins from cyclic acid. After dehydration, esterification, reduction, sulfidation, grignard, carboxylation, reduction, ring-opening and ring-closing reaction, ### is generated.

Process B is used by Zhejiang #### and Zhejiang #### and its production pathway is as follow:

.....

Source: CCM international Ltd

Process B uses new chiral amine-(1S,2S)-1-(4-nitrophenyl)-2-(N,N-dimethylamino)-3-tribenzoylmethoxy-1-propanol, which could be made by Zhejiang #### & Zhejiang #### themselves. This chiral amine is more active than (1S,2S)-(+)-threo-1-(p-nitrophenyl)- 2-amino-1,3-propanediol.

It is the major and the most advanced technology now. So many researchers, including Professor #### Chen, do a lot of researches on it. Its disadvantages and some improvements are showed as following:

✧ Reaction B has high yield rate, but (1S,2S)-1-(4-nitrophenyl)-2-(N,N-dimethylamino)-3-

tribenzylmethoxy-1-propanol is hard to produce. Professor ##### Chen tries to use 9- propargyl quinine to substitute it.

- ✧ Reaction E needs a strictly required reaction condition and there are a lot of side reactions. Professor ##### Chen uses Zn and 5-bromovalerate to react with substrate (Fukuyama reaction) under the catalyzing of Pd to substitute the Grignard and carboxylation reaction.
- ✧ Reaction F needs high H₂ pressure and reaction with high temperature. At the same time, it needs Pd, which is expensive, to catalyze reaction. Besides, the sulphur in substrate is toxic to Pd, and then some side reactions happen, which makes yield rate reduced.
- ✧ Reaction G needs long reaction time and there are a lot of side reactions. The product- (2S,3S,4S)-5-(3,4-diamino-tetrahydrothiophene-2-)pentanoic acid halogen acid salts, in yellow color, has some impurity and HBr. It is easy to be damaged and HBr makes it decomposed.
- ✧ Reaction H needs a lot of Triphosgene.

The yield rate of each reaction mentioned above are quite satisfying which makes the total yield rate reach 41.92 %, based on cyclic acid.

Table I-2.4.2-1 Yield rate of each reaction of Process B

Reaction NO.	Reaction Name	Yield rate
A	Dehydration Reaction	***
B	Esterification Reaction	***
C	Reduction Reaction	***
D	Sulfidation Reaction	***
E	Grignard, Carboxylation Reaction	***
F	Reduction Reaction	
G	Ring-Opening Reaction	***
H	Ring-Closing Reaction	***

Figure II-2.4.2-1 Flow chart of Process B

.....

Source: CCM

➤ Production mode

Table I-2.4.2-2 Estimation on raw material cost for Process B

Raw Material	Consumption unit / kg ###		Unit	Price RMB/Unit	Unit cost, RMB/kg ###	
	Min.	Max.			Min	Max
#####	xxx	xxx	kg	xxx	xxx	xxx
#####	xxx	xxx	kg	xxx	xxx	xxx
#####	xxx	xxx	kg	xxx	xxx	xxx
#####	xxx	xxx	kg	xxx	xxx	xxx
#####	xxx	xxx	L	xxx	xxx	xxx

####	xxx	xxx	kg	xxx	xxx	xxx
####	xxx	xxx	kg	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
####	xxx	xxx	L	xxx	xxx	xxx
Others				xxx	xxx	xxx
Total					1,916.88	2,397.25

Note: According to the boiling point and polarity of solvents, CCM gives different solvent 70%~ 90% recycle rate. The recycle rate of Pd-D296 is 90%.

Source: CCM

I-3 Player Analysis

I-3.1 Zhejiang ##### Co., Ltd.

I-3.1.1 Introduction

In 1999, Zhejiang ##### bought the technology-Process A from Professor ##### Chen, at the price of several million yuan. But Zhejiang ##### thought Professor ##### Chen was careless in protecting the technology and let it leaked to other company. At last, it did not pay money to Professor ##### Chen for the technology. Then, Professor ##### Chen did not help Zhejiang ##### to improve its technology. So Zhejiang ##### carries out most of the technology innovation and improvement by itself. It is reported that Zhejiang ##### only use 8 steps in the synthesis of ###, instead of 11 reaction steps in Roche.

In October 2001, Zhejiang ##### started the commercial production of ### with capacity of 10t/a. With mild reaction conditions, its production cost is low and the raw materials are easy to be obtained. At that time, its production cost was only 1/3 of Roche's and the total yield rate was about 12%.

In 2002, because ### sold well in 2001, Zhejiang #### constructed a new workshop to produce ###, with the investment of 6.9 million yuan. The company's ### production capacity increased from 20t/a to 30t/a.

On September 26th, 2002, the first State Level Feed Engineering Technology Research Center ### Production Base was established in Zhejiang #### .

Zhejiang #### has planned to develop its technology since 2003 to improve product quality, with aim to achieve high purity and no toxicity, raise output, save energy and reduce production cost.

Mr. Jia####i Chen, the vice plant manager of synthesis plant of Zhejiang ####, is the leader of the research team in synthesis plant of Zhejiang #### and is engaged in the research of ###.

There is still some other information about ### in Zhejiang ####.

- Professor #### Chen claims Zhejiang #### is still adopting the technology which was developed by him in 1999.
- Via asymmetric separation induced by chiral amine, improved Grignard reaction, stereospecific hydrogenation and ring-closing reaction by Triphosgene, Zhejiang #### synthesized ### with the optical purity of over 99%.
- Mr. Jia####i Chen has also researched on the production of Potassium Thioacetate, Key side Chain of ###, raw material-Cyclic acid, Potassium borohydrid etc. And these raw materials have come into commercial production in Zhejiang Kinglyuan Pharmaceutical Company Limited, Zhejiang Guobang Pharmaceutical Co., Ltd., Zhongning Chemical Co., Ltd. and Zhejiang Sixian Pharmaceutical Co.,Ltd.
- Zhejiang #### has improved its production line according to Green Chemical Concept. It accomplished nonpolluting production by changing production condition, changing solvents, recycling solvents and utilizing by-product.
- One kg ### production needs 4~5 kg cyclic acid. The cost of cyclic acid accounts for over 50% of the total manufacture cost.
- Zhao Wang, professor of Zhejiang University of Technology, has a team to help Zhejiang #### improve its ### technology. His team researches on not only fermentation method but also chemical synthesis method. The major research is how to transfer (4S, 5R) into (4R,5S) by fermentation method. Now, the transfer rate is only 20%.

Apply Number	Name
CN2003	Production method
CN2003	Production method of.....
CN2003	Production method of a kind of
CN2003	Production method of
CN2006	Production method of
CN2006	Synthesis method of
CN2006	Purification of

CN2006	Synthesis method of.....
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Mr. Jia#####i Chen has the following patents which are related to ###:

Source: CCM

Figure II-3.1.1-1 Flow chart of synthesis process of ### in Zhejiang #####

.....

Source: CCM international Ltd

I-3.1.2 Profit estimation of

➤ Raw material cost estimation

Based on the information mentioned above, we understand that Zhejiang #####'s production process of ### is similar to Process A. We made some emendations of the model and the estimated raw material costs are shown in the following table.

Table I-3.1.2 -1 Estimation on raw material cost of ### in Zhejiang ##### in September 2008

No.	Raw Materials	Consumption, unit / kg ###	Unit	Price, RMB/unit	Unit cost, RMB/kg ###
1	#####	###	kg	###	###
2	#####	###	kg	###	###
3	#####	###	kg	###	###
4	#####	###	kg	###	###
5	#####	###	kg	###	###
6	#####	###	kg	###	###
7	#####	###	kg	###	###
8	#####	###	L	###	###
9	#####	###	L	###	###
10	#####	###	kg	###	###
11	#####	###	L	###	###
12	#####	###	kg	###	###
13	#####	###	kg	###	###
14	#####	###	kg	###	###
15	#####	###	kg	###	###
16	#####	###	kg	###	###
17	#####	###	kg	###	###
18	#####	###	g	###	###
19	#####	###	g	###	###
20	#####	###	L	###	###
21	#####	###	L	###	###
22	#####	###	L	###	###
23	#####	###	L	###	###

24	####	###	L	###	###
25	####	###	kg	###	###
26	####	###	L	###	###
27	####	###	kg	###	###
28	####	###	kg	###	###
29	####	###	L	###	###
30	####	###	kg	###	###
31	####	###	L	###	###
32	####	###	L	###	###
33	Others	###		###	###
	Total				2,434.02

Note: According to the boiling point and polarity of solvents, CCM gives different solvent 70%~ 90% recycle rate. The recycle rate of Pd-D296 is 90%.

Source: CCM

➤ Estimation of manufacturing costs

Table I-3.1.2-2 Estimation on manufacturing cost of ### in Zhejiang #### in September 2008

No	Item		Unit Cost: RMB/ kg ###
1	Raw Materials		###
2	Utilities	Water	###
		Electric power	###
		Steam	###
3	Labor		###
4	Packing		###
5	Manufacturing direct + indirect*		###
	Total		2,583.59

Note:* The manufacturing direct and indirect costs are assumed to be the fixed costs, which include depreciation, maintenance, etc. Manufacturing direct and indirect*=Maintenance fee+ depreciation

Source: CCM

➤ Estimation of management cost

In China, the following costs are regarded as management cost:

- ✓ Salary cost of management staffs and other auxiliary staffs
- ✓ Materials cost for management
- ✓ Financial cost (such as loan interest)
- ✓ Transportation cost
- ✓ Distribution cost

It is difficult to give a detailed estimation on the management cost of ### in most domestic producers at

the moment. There are mainly two reasons for this.

- ✓ The sales value of ### is relatively small compared with that of the other products in these companies. For instance, it only accounts for less than 10% of Zhejiang ####'s total sales value currently. So some items such as material cost for management, financial cost and distribution cost can not be found in these companies' financial report.
- ✓ The production capacities and management structures vary a lot between different manufacturers in China.

Based on the estimation of other companies, CCM estimates that the management cost of ### production is about 10% of the production cost. So the management cost of Zhejiang #### is estimated to be RMB287.07/kg (USD41.97/kg).

➤ Estimation of total production cost

The total cost of production is the sum of the manufacturing cost and the management cost.

Table I-3.1.2-3 Estimation on total production cost of ### in Zhejiang #### in September 2008

Item	Cost (RMB/kg ###)
Manufacturing cost	###
Management cost	###
Total production cost	###

Source: CCM

➤ Profit estimation of

Before making the profit estimation, there are some backgrounds in China that need to be taken into account:

- ✓ The VAT (value added tax) in China is 17%
- ✓ The Chinese government encourages the export of some products, by returning certain percentages of VAT to the exporter. But this percentage cannot exceed 17%.

In addition, there is some basic information in understanding Chinese situation:

▪ Taxes

- Value Added Tax (VAT): 17%

VAT paid=Ex-Factory Price ÷1.17x17% - Materials Cost ÷1.17x17% - Utility Cost ÷1.17x17%

EAT &CT= VAT x 10 %

▪ The return of VAT for exported

Since Chinese government encourages the export of some products produced in the domestic market.

17% of the VAT paid will be refunded to the ### exporter.

Return of VAT = Ex-Factory Price ÷ 1.17 × 17%

Based on the data mentioned above, the profit of ### in Zhejiang #### can be estimated and shown in the following table.

Table I-3.1.2-4 Estimation on profit of ### in Zhejiang #### in September 2008

Item	RMB / kg ###	Remark
1.Income	###	Sales price + Return of VAT
Price	###	Sales price of ### in the domestic market
Return of VAT	###	Ex-Factory Price/1.17×17%
2.Expense	###	
Production cost	###	From the calculation
VAT	###	Ex-Factory Price □ 1.17×17%- Materials Cost □ 1.17×17%- Utilities Cost □ 1.17×17%
EAT & CT	###	VAT x 10 %
3.Gross Profit	###	Income – Expense
4.Profit tax	###	Gross Profit x 25 %
5.Profit after tax	7,008.31	Gross Profit – Profits Tax

Source: CCM

I-3-2 Zhejiang #### Pharmaceutical CO., Ltd.

I-3.2.1 Introduction

After acquiring the ### production technology, Zhejiang #### invested 120 million yuan in constructing production line of ### in Potang Industry Zone and began to produce ### in 2002 with capacity of 10t/a.

At the beginning, the production was not stable due to immature technology. At that time, the production was only dozens of kg/month. However, in 2004, Zhejiang #### improved its technology and made the production cost reduced 70%.

Nowadays, its technology is the most advanced in the world. Professor #### Chen and Wenzhou Huaji claim that Zhejiang #### has the best technology. Wenzhou Huaji claims that 3~4 kg cyclic acid is needed to produce one kg ### in Zhejiang ####. A####i Langxi claims the production cost of Zhejiang #### is lower than RMB 2,000/kg ###.

In 2005, its sales value of ### was 40 million yuan.

Its aim is to be the one of the top 2 ### manufacturers in China before 2009.

Its flowchart is similar to the Process B.

I-3.2.2 Profit estimation of

➤ Raw material costs estimation

Based on the information mentioned above, we understand that Zhejiang ####'s production process of ### is similar to Process B. We made some emendations of the model and the raw material costs are shown in the following table.

Table I-3.2.2 -1 Estimation on raw material cost of ### in Zhejiang #### in September 2008

No.	Raw materials	Consumption, unit / kg ###	Unit	Price, RMB/Unit	Unit cost, RMB/kg ###
1	###	###	kg	###	###
2	###	###	kg	###	###
3	###	###	kg	###	###
4	###	###	kg	###	###
5	###	###	L	###	###
6	###	###	kg	###	###
7	###	###	kg	###	###
8	###	###	L	###	###
9	###	###	L	###	###
10	###	###	L	###	###
11	###	###	L	###	###
12	###	###	L	###	###
13	###	###	L	###	###
14	###	###	L	###	###
15	###	###	g	###	###
16	###	###	L	###	###
17	###	###	L	###	###
18	###	###	L	###	###
19	###	###	L	###	###
20	###	###	L	###	###
21	###	###	kg	###	###
22	###	###	L	###	###
23	###	###	L	###	###
24	###	###	g	###	###
25	Others	###		###	###
	Total	###		###	1,910.57

Note: According to the boiling point and polarity of solvents, CCM gives different solvent 70%~ 90% recycle rate. The recycle rate of Pd is 95%.

Source: CCM international Ltd

➤ **Estimation of manufacturing costs**

Table I-3.2.2-2 Estimation on manufacturing cost of ### in Zhejiang ##### in September 2008

No	Item	Unit Cost RMB / kg ###	
1	Raw Materials	###	
2	Utilities	Water	###
		Electric power	###
		Steam	###
3	Labor	###	
4	Packing	###	
5	Manufacturing direct + indirect*	###	
	Total	2,082.56	

Note:* The manufacturing direct and indirect costs are assumed to be the fixed costs, which include depreciation, maintenance, etc. Manufacturing direct and indirect*=Maintenance fee+ depreciation

Source: CCM

➤ **Estimation of management cost**

Based on the estimation on other companies, we estimate that the management cost of ### production in Zhejiang ##### is about 10% of the production cost. So the management cost of Zhejiang ##### is estimated to be RMB231.40/kg (USD 33.83/kg).

➤ **Estimation of total production cost**

The total cost of production is the sum of the manufacturing cost and the management cost.

Table I-3.2.2-3 Estimation on total production cost of ### in Zhejiang ##### in September 2008

Item	Cost, RMB/kg ###
Manufacturing cost	###
Management cost	###
Total production cost	2,313.95

Source: CCM

➤ **Profit estimation of ###**

Based on the data mentioned above, the profit of ### in Zhejiang ##### can be estimated and shown in the following table.

Table I-3.2.2-4 Estimation on the profit of ### in Zhejiang ##### in September 2008

No.	Item	RMB / kg ###	Remark
-----	------	--------------	--------

1	Income	###	Sales price + Return of VAT
	Price	###	Sales price of ### in the domestic market
	Return of VAT	###	Ex-Factory Price ,1.17x15%
2	Expense	###	
	Production cost	###	From the calculation
	VAT	###	Ex-Factory Price ,1.17x17% - Materials Cost ,1.17x17% - Utilities Cost ,1.17x17%
	EAT & CT	###	VAT x 10 %
3	Gross Profit	###	Income – Expense
4	Profit tax	###	Gross Profit x 25 %
5	Profit after tax	7,363.03	Gross Profit – Profits Tax

Source: CCM

I-3-3 Zhejiang ##### Co., Ltd.

I-3.3.1 Introduction

Zhejiang ##### began to produce ### in 2002, but it stopped production for a period. Then it acquired the technology without the permission of Zhejiang ##### in 2003 and it began commercial production in 2006. So its flowchart is similar to the Process B.

Zhejiang ##### cooperates with Haoran Li, Professor of Zhejiang University, in many product researches, such as VA. And Haoran Li researched on ### in 2001~2002. Whether he is still researching on ### or not is unknown.

Haoran Li, together with Zhejiang #####, has a patent about how to recycle the Mg ion and Br ion in waste water of Grignard reaction.

I-3.3.2 Profit estimation of

➤ Raw material cost estimation

Zhejiang #####'s production process of ### is similar to Process B. We made some emendations of the model and the raw material costs are shown in the following table.

Table I-3.3.2 -1 Estimation on raw material cost of ### in Zhejiang ##### in September 2008

No.	Raw Materials	Consumption, Unit / kg ###	Unit	Price, RMB/Unit	Unit Cost, RMB/kg ###
1	#####	#####	kg	#####	#####
2	#####	#####	kg	#####	#####
3	#####	#####	kg	#####	#####

4	####	####	kg	####	####
5	####	####	L	####	####
6	####	####	kg	####	####
7	####	####	kg	####	####
8	####	####	L	####	####
9	####	####	L	####	####
10	####	####	L	####	####
11	####	####	L	####	####
12	####	####	L	####	####
13	####	####	L	####	####
14	####	####	L	####	####
15	####	####	g	####	####
16	####	####	L	####	####
17	####	####	L	####	####
18	####	####	L	####	####
19	####	####	L	####	####
20	####	####	L	####	####
21	####	####	kg	####	####
22	####	####	L	####	####
23	####	####	L	####	####
24	####	####	g	####	####
25	Others	####		####	####
	Total				2,057.52

Note: According to the boiling point and polarity of solvents, CCM gives different solvent 70%~ 90% recycle rate. The recycle rate of Pd is 95%.

Source: CCM

➤ Estimation of manufacturing costs

Table I-3.3.2-2 Estimation on manufacturing cost of ### in Zhejiang #### in September 2008

No	Item	Unit cost: RMB/ kg ###	
1	Raw Materials	####	
2	Utilities	Water	####
		Electric power	####
		Steam	####
3	Labor	####	
4	Packing	####	
5	Manufacturing direct + indirect*	####	
	Total	2,203.83	

Note:* The manufacturing direct and indirect costs are assumed to be the fixed costs, which include depreciation, maintenance, etc. Manufacturing direct and indirect* = Maintenance fee + depreciation

Source: CCM international Ltd

➤ **Estimation of management cost**

Based on the estimation on other companies, CCM estimates that the management cost of ### production is about 10% of the production cost. So the management cost of Zhejiang ##### is estimated to be RMB244.87/kg (USD35.80/kg).

➤ **Estimation of total production cost**

The total cost of production is the sum of the manufacturing cost and the management cost.

Table I-3.3.2-3 Estimation on the total production cost of ### in Zhejiang ##### in September 2008

Item	Cost, RMB/kg ###
Manufacturing cost	####
Management cost	####
Total production cost	2,448.70

Source: CCM

➤ **Profit estimation of ###**

Based on the data mentioned above, the profit of ### in Zhejiang ##### can be estimated and shown in the following table.

Table I-3.3.2-4 Estimation on profit of ### in Zhejiang ##### in September 2008

No.	Item	RMB / kg ###	Remark
1	Income	13,743.59	Sales price + Return of VAT
	Price	####	Sales price of ### in the domestic market
	Return of VAT	####	Ex-Factory Price □ 1.17x15%
2	Expense	####	
	Production cost	####	From the calculation
	VAT	####	Ex-Factory Price □ 1.17x17% - Materials Cost □ 1.17x17% - Utilities Cost □ 1.17x17%
	EAT & CT	####	VAT x 10 %
3	Gross Profit	####	Income – Expense
4	Profit tax	####	Gross Profit x 25 %
5	Profit after tax	7,279.58	Gross Profit – Profits Tax

Source: CCM

I-3.4 Comparison of manufacturers

CCM makes a comparison between the three major manufacturers of ### in China.

Table I-3.4-1 Comparison of the three ### manufacturers

Company	Zhejiang ###	Zhejiang ###	Zhejiang ###
Advantage	First ### producer in China, Has pharmaceutical product, Largest capacity in the world	Advanced technology	Advanced technology
Disadvantage	Technology is inefficient	Low capacity Low total asset	
Production of ### from	2001	2002	2006
Technology	Inefficient	The best	Efficient
Research ability	Strong	Strong	Strong
Listed company	Yes	No	Yes
Capacity in 2007	50t/a	20t/a	30t/a
Output in 2007	30 tonnes	18 tonnes	25 tonnes
Sales volume of ### in total sales volume in 2007	7.51%	Major product	7.20%
Pharmaceutical product	Produce	Not produce	Not produce
Price (RMB/kg ###)	12,000	12,000	12,000
Production cost (RMB/kg ###)	2,859.55	2,302.84	2,437.59
Profit after tax (RMB/kg ###)	6,967.02	7,327.44	7,242.40
Net profit margin	58.06%	61.06%	60.35%
Total asset	820 million yuan	160 million yuan	880 million yuan
Quality	Good	Good	Good

Source: CCM

Zhejiang ### has the most advanced technology and the lowest production cost in the world. Though its capacity is low now, it has ability to enlarge its capacity. It is expected to become the most competitive manufacturer in China in the future.

Zhejiang ###'s technology is inefficient and it suspended production for several months in 2008. And its output is reducing. But it does not plan to give up ###. Zhejiang ### has cooperated with Zhao Wang to recycle the by-product in ### production to reduce production cost.

I-4 Tel interview and site visit with Professor ### Chen

Tel:

Person to contact: Professor ### Chen (Professor)

Professor Chen is the chief person in charge of the research for ###. He has done research on it for over ten years. The following information is the telephone interview and site visit with Professor Chen.

- **Production Technology Opinions**

Up to 1999, Professor ##### Chen's technology has been transferred to Zhejiang #####. But one of Professor ##### Chen's students leaked this technology, and then Zhejiang ##### thinks it was the fault of Professor ##### Chen. At last, Zhejiang ##### did not pay for Professor ##### Chen's technology.

Due to the conflict between Professor ##### Chen and Zhejiang #####, ##### Chen wants to transfer his technology to a large company that has ability to wash out Zhejiang ##### from the market.

He discloses the #### production cost of Zhejiang ##### was around RMB3,000~4,000/kg in 2003. At present, Zhejiang #####'s technology has been improved and the cost is reduced to over RMB2,000/kg. Though Zhejiang ##### has researched a lot on ###, its technology is still the old technology which was transferred from him in 1999 and it is inefficient.

Up to 2002, his new technology had been transferred to Zhejiang #####, which made Zhejiang ##### have the most advanced technology.

In 2003, Zhejiang #####'s technology was leaked to Zhejiang #####

At the same time, ##### Chen is still researching on new technology of ### production. After transfer another technology to Zhejiang #####, he has developed another new technology now which has not been transferred yet. This new technology can make the production cost lower than RMB2,000/kg.

All the ### production process in China doesn't begin with fumaric acid but cyclic acid now. He comments that it is because cyclic acid can be purchased from other factories thus it is not necessary for ### producers to produce cyclic acid. Shanghai Desano has no fixed cyclic acid supplier and it may produce cyclic acid itself.

The production is in batch production and it needs no continuous production.

Without land and technology, the investment is around 8~10 million yuan as to a production line of 50t/a ###. If land is taken into account, 10~20 million yuan will be enough. It is better to be constructed on the base of chemical pharmaceutical factory. To enlarge capacity needs only a little money.

The domestic development is in the process of improving product quality, increasing yield, saving energy, reducing production cost and how to produce ### in room temperature and atmospheric pressure.

Yield rate, reaction steps and reaction time are all not so important. The most important factor is the production cost. If one manufacturer can not handle the solvent recycling well, the solvent cost may be higher than the raw materials.

To estimate whether a technology is good, manufacturers should pay attention to the quality of product,

production cost, environmental protection, etc.

Of course, the production has some pollution, but Chen focuses on how to recycle solvent to reduce pollution and cost.

The cost of water, electricity and gas is very low.

In production, Pd is needed. Pd can be recycled. Good manufacturers can recycle all the Pd. If there is little Pd that can not be recycled, it can be used in the next batch production.

After getting his technology, manufacturers should do a lot of improvement.

- **Market Opinions**

Professor ##### Chen is strongly confident about his technology and considers that technology is the most crucial factor in ### production. According to Chen, his technology has made Roche give up ### production before, and now his technology can make other manufacturers give up ### production too.

In 2001, the market of ### was active. At that time, the ### price reached around USD5,000/kg.

In 2003, the market situation was not so active as before because there were too many producers to produce ###. The product is over-supplied.

- **Domestic Producers**

Chen does not help Zhejiang ##### to improve its technology and Zhejiang #####'s technology is inefficient now.

As to Zhejiang #####, its technology is the most advanced now in China.

As to Shanghai Desano, one of his student, a female postgraduate, has leaked his technology to Shanghai Desano. But the leaked information on the technology is only a small part of the whole technology information. Now, this leaked technology hasn't been applied to the commercial production in Shanghai Desano. Shanghai Desano's current technology is obtained from DSM.

- **Fermentation technology**

In addition, Professor ##### Chen thinks domestic fermentation technology is immature, which can't be used in industrial production. Hubei Guangji Pharmaceutical Co.,Ltd tried to produce ### via fermentation method. Professor ##### Chen ever contacted it and provided his advice, but Hubei Guangji Pharmaceutical Co.,Ltd didn't take his advice. Now, the company has stopped this production trial.

-----The end of the report-----

Contact us

To learn more information about CCM's end use analysis service, please contact us by econtact@cnchemicals.com.